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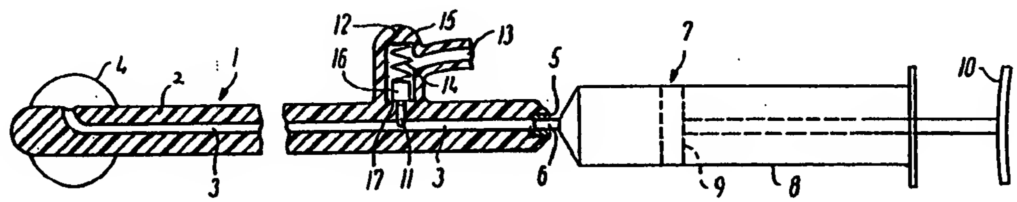

(57) Abstract

The present invention relates to a balloon catheter comprising at least one inflatable balloon and a fluid inlet for injecting fluid into the balloon or a device adapted to be connected to a balloon catheter with at least one inflatable balloon and a fluid inlet for injecting fluid into the balloon which device has at least one channel for fluid which channel, when connected to a balloon catheter, is in communication with the inlet or an outlet from the balloon catheter. The balloon catheter or the device comprises a relief or by-pass valve means placed in or in connection with a channel for fluid, which relief or by-pass valve means normally is closed, but open when the balloon pressure reaches a predetermined level, so that further injected fluid can escape through the relief or by-pass valve.

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A balloon catheter or a device to be used together with a balloon catheter

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The present invention generally relates to medical inflatable devices and, more particularly, to a balloon catheter or a device to be used together with a balloon catheter, which balloon catheter or device limits the pressure in the balloon or the balloons to a desired level while the balloon or the balloons are inflated.

Balloon catheters are indispensable devices in medical and surgical treatment of diseases in hollow tubular organs in the animal as well as in the human body. Examples of tubular organs are bladders, bile ducts, oesophagus, urethra, ureter, and those of the genital system.

In addition, many internal organs, e.g. the brain, heart, liver, kidneys, and pancreas possess true spaces such as cavities, cavernous sinuses, lumens, etc. Also diseases from necrotic tumors or traumatic injuries may create spaces within otherwise solid organs.

A variety of balloon catheters for use in the human body are known, e.g. urethral, hemostatic, fiberscope, endotracheal, embolectomy, and angioplasty balloon catheters. Embodiments of such balloon catheters have been disclosed in e.g. the following US patent specifications:

Nos. 5 502 238, 2 210 744, 2 687 131, 2 799 273, 4 022 216, 4 224 929, 4 295 464, 4 327 720, 4 423 725, 4 430 083, 4 624 657, 4 627 837, 4 696 668, 4 705 502, 4 751 924 and 4 755 176.

Due to the high standard of living and longevity the occurrence of atherosclerotic diseases from stenosed and

occluded arteries have soared during recent years.

In 1964, the American radiologist Charles Dotter introduced a method for arterial revascularization by means of straight coaxial catheters with increasing diameters introduced percutaneously in atherosclerotic arteries (Dotter 1964). Ten years later, Andreas Grüntzig from Switzerland reported improved revascularization potential and safety of the Dotter technique using a balloon catheter for dilatation of atherosclerotic arterial obstructions (Grüntzig 1974). This so-called balloon angioplasty catheter consists of a catheter shaft. At the distal end of the shaft an oblong balloon which can be inflated with fluid at high pressures to a predetermined maximal diameter, is mounted. Hereby, atherosclerotic obstructions can be dilated with a minimum risk of arterial rupture.

The revascularization method envisioned by Dotter, and the balloon angioplasty catheter later invented by Grüntzig founded the field of endovascular surgery which has spread tremendously world-wide, and today is used for revascularization of atherosclerotic and obstructed arteries from head to heel (Becker 1989). In 1990, more than 400 000 endovascular treatments were performed in USA (Gaylord 1991), whereas the figure world-wide remains unknown. Balloon angioplasty is also used in non-atherosclerotic diseases, e.g. fibromuscular dysplasia of renal arteries, and aortic coarctation.

Various improved balloon angioplasty catheters have been developed for percutaneous transluminal angioplasty (PTA) of obstructed peripheral arteries, and for percutaneous transluminal coronary angioplasty (PTCA) of obstructed arteries of the heart. Such catheters have been described in e.g. US patent specifications Nos. 4 271 839, 4 723

549, 4 744 366, 4 763 654 and 4 771 777 and in EP patent applications Nos. 379 794 and 429 522. In addition, balloon dilatation procedures are used therapeutically in diseases of e.g. the bile ducts and the prostate. Balloon occlusion procedures are known in e.g. hemostasis of bleeding oesophageal varicose veins often associated with cirrhosis of the liver.

The PTA procedure is initiated by making a skin puncture with a needle, and subsequently introducing a guide-wire or a guiding catheter into the artery through the needle, whereafter the needle is removed (Seldinger technique). The guide-wire or the guiding catheter is traversed the obstructions, whereafter a balloon angioplasty catheter is passed over the guide-wire or through the guiding catheter. The balloon angioplasty catheter has the balloon totally deflated by negative pressure, as it is advanced inside the target artery towards the point of arterial obstruction intended for dilatation when the balloon portion of the catheter is properly positioned inside the obstructed arterial segment, under X-ray fluoroscopic, the balloon is inflated by injection of fluid contrast media at a pressure sufficient to overcome the resistance of the atherosclerotic obstruction. The balloon pressure required to exert sufficient force for dilatation of athero-sclerotic obstructions is usually 5-10 positive atmospheres. In case of e.g. stenosed vein grafts, balloon pressures of 10-20 positive atmospheres are usually needed to obtain effective dilatation.

By one or more balloon inflations over periods from 20-30 seconds to one or two minutes (allowing blood flow between inflations) at the above-mentioned balloon pressures, including appropriate relocations of the balloon between inflations in obstructions longer then the balloon itself, the desired dilatation of the obstructed arterial segment

can be achieved. Hereafter, the balloon is completely deflated, and the guide-wire or the guiding catheter and the balloon catheter are withdrawn from the artery. The procedure is terminated with hemostasis obtained by manual compression of the puncture site.

In spite of the fact that balloon angioplasty has gained widespread use in the treatment of atherosclerotic arteries of the lower limbs, the heart and elsewhere, and to some extent has replaced coronary and peripheral bypass surgery by endovascular surgery, the results of balloon angioplasty are not entirely satisfactory. The unacceptable high rate of technical failures due to guide-wire resistance at the vascular obstruction, especially occlusions, is decreasing as a result of improved guide-wires (Morgenstern 1989) and high technology recanalization devices such as lasers, drills, and ultrasonic probes developed through recent years (Cragg 1989, Snyder 1988, Siegel 1989). A more important, and largely unsolved problem, is failure of balloon angioplasty due to rethrombosis which may occur in up to 40% of femoropopliteal arteries within hours of dilatation (Jørgensen 1990), and restenosis which occurs in 30%-50% of arterial obstructions within the first 6-12 months of their dilatation (Gallino 1984, Krepel 1985, Johnston 1987, Jørgensen 1991a).

Early or late failure of otherwise completed balloon angioplasty procedures relates to their inherently injuring effects to the arterial wall. Luminal expansion of atherosclerotic arterial obstructions by PTA does not rely on compression of the atherosclerotic material which is incompressible (Block 1980), but depends on fracturing of the calcified intima and subsequent stretching of the deeper medial and adventitial layers (Kinney 1984). By this mechanism of action, PTA produces deep arterial wall

injuries (Lyon 1987) which activate platelets and the coagulation pathways leading to thrombin formation and mural thrombosis (Chesebro 1991). The risk of intraluminal thrombosis, and subsequent thrombotic reocclusion of arterial segments within hours of dilatation increases with decreasing arterial diameter, and is reported more prevalent after PTA for occlusions than for stenoses (Jørgensen 1990, Jeans 1990).

The thrombotic response to PTA was first investigated by Blättler and co-workers, who reported increased levels of beta-thromboglobulin (BTG) indicating platelet activation during and after dilatation (Blättler 1983), and increased levels of fibrinopeptide A (FPA) indicating thrombin activity on fibrinogen and thus intravascular fibrin formation in patients not receiving heparin during PTA (Blättler 1986). They also reported that an intra-arterial 5000 IU heparin bolus injection during PTA could eliminate the BTG and FPA increase measured in peripheral blood. These findings gave a solid argument for the widespread use of heparin as a preventive measure against rethrombosis in conjunction with balloon angioplasty procedures. Although heparin may reduce markers of platelet activation and thrombin activity in peripheral blood, this effect appeared, however, not to preclude rethrombosis after PTA.

The inventor of the present invention was the first to publish a study demonstrating a significantly increased risk of post-PTA rethrombosis in femoropopliteal occlusions as opposed to stenoses in heparin treated patients (Jørgensen 1990). This finding has been confirmed by later studies (Jeans 1990). Subsequently, it was demonstrated that PTA produces intense thrombin activity at dilated sites which is not expressed in peripheral blood, corresponding to the findings of a 50-fold

intra-arterial FPA increase in the vicinity of dilated sites simultaneous with only a 2-fold FPA increase in peripheral blood (Jørgensen 1992a). Preliminary results of ongoing studies indicate that intra-arterial administration of 5000 IU heparin bolus injections only partly reduces the intra-arterial FPA increase found during PTA (Jørgensen, unpublished data). These findings warranted another regimen than conventional heparin bolus administration for appropriate elimination of thrombin activity at dilated sites after PTA, should rethrombosis be prevented. In PTCA, the rate of rethrombosis is 5%-10% and generally lower than in PTA due to full heparinization of patients undergoing PTCA (Cowley 1988).

Such a regimen is commenced by a bolus injection of 15000-25000 IU heparin followed by intravenous infusion of 1000 IU heparin per hour, and is not used in PTA due to the risk of bleeding complications.

The above-mentioned difference in post-PTA rethrombosis rate may relate to larger amounts of preexisting thrombus in occlusions than in stenoses, as reported in PTCA (Mabin 1985). During balloon dilatation of a thrombotic obstruction, fibrin-bound thrombin with preserved procoagulant activity is released by the balloon compression and disintegration of the thrombus (Francis 1983). After dilatation, thrombus residues cover the inside of the vessel wall and make an extremely thrombogenic surface which in addition to the deep injury may help to explain the prevalence of early rethrombosis reported after PTA in femoropopliteal occlusions.

When rethrombosis develops after PTA, it may be treated by intra-arterial infusion of thrombolytic agents such as streptokinase (SK) (Graor 1985) or tissue-type plasminogen activator (t-PA) (Graor 1986). Other thrombolytic agents

commercially available at present include urokinase (UK), single-chain urokinase-type plasminogen activator (scu-PA), anisoylated plasminogen streptokinase activator complex (APSAC), and two-chain urokinase-type plasminogen activator (tcu-PA). In addition, rethrombosis after PTA could probably be treated with thrombin inhibitors such as heparin and related substances (Heras 1988), hirudin (Heras 1990), and activated protein C (Runge 1990). Most of the substances mentioned are available in recombinant forms. There is little doubt that future investigations and biogenic engineering will provide new compounds applicable in the treatment of thrombosis (Runge 1991).

Following the recognition by the inventor of the present invention of patients with femoropopliteal occlusions as a subset with significantly increased risk of rethrombosis after PTA, it became mandatory to consider new treatment modalities for prevention rather than treatment of rethrombosis in high-risk patients.

The inventor of the present invention subsequently participated in the development of segmentally enclosed thrombolysis (SET) which is a new thrombolytic technique launched for prevention of rethrombosis after balloon dilatation procedures (Jørgensen 1989). The basic principle of SET is dissolution of residual thrombus immediately after PTA and prevention of subsequent formation of new thrombus at dilated sites. High efficacy and rapidity of the procedure should be achieved by using very high concentrations of thrombolytic and anti-thrombin agents such as t-PA and heparin. If accumulated in the general circulation, such high agent concentrations would inevitably lead to bleeding complications. Even with standard regimens, thrombolytic agents accumulate in the general circulation during intra-arterial infusion, and conventional thrombolytic therapy of peripheral arteries

carry a low, but serious risk of fatal hemorrhages due to depletion of coagulation factors during drug infusion (Ricotta 1987, Urban 1992). However, if the agents could be enclosed in dilated arterial segments, only a small dose would be needed to obtain a vast local concentration, general infusion would be avoided, and the risk of bleeding complications would probably be reduced.

According to the technique hitherto employed, SET is performed in an arterial segment which has been subjected to balloon angioplasty just before. The arterial segment is subsequently secluded by simultaneous inflation of two balloons of a double-balloon catheter placed with a balloon at each end of the segment. Low doses of t-PA (5 mg) and heparin (1000 IU) are injected through a channel opening between the balloons, and are enclosed in the secluded arterial segment for a suitable period of time (e.g. 30 minutes during SET), whereafter the catheter is removed. Using this method it is possible to perform local treatments of arterial segments with high concentrations of t-PA and heparin without exposing the general circulation to similarly high concentrations. The treatment time with SET is short when compared to 6 or more hours with systemic thrombolytic therapy (Earnshaw 1988), but even more important, the effect of the locally applied agents continues for hours or days after termination of SET. Due to this and other remarkable features of SET performed with t-PA and heparin in atherosclerotic arteries after PTA, a wide range of studies on treatments with a variety of pharmacological agents segmentally enclosed with double-balloon catheters in different tubular body organs are likely to be expected, and may well pave the way for new therapeutical approaches developing in the near future.

The inventor of the present invention has conducted a number of pilot studies in order to evaluate clinical and biochemical effects of SET applied as an adjunct to femoropopliteal PTA. Published data indicate that thrombolytic therapy performed as SET is safe in terms of bleeding complications, and SET does not lead to depletion of coagulation factors (Jørgensen 1991b). Furthermore, SET reduced the rate of rethrombosis after PTA for femoropopliteal occlusions by approximately 75% compared with previous results (Jørgensen 1991b). The reduction in rethrombosis rate followed a complete elimination of the intense intraarterial thrombin activity produced by PTA and otherwise present at dilated sites shortly after (Jørgensen 1992a). The average t-PA concentration retained between the balloons of the double-balloon catheter was about 30.000 ng/ml or 20 times higher during SET than steady-state concentrations obtained during systemic infusion. At the same time, the t-PA concentration in peripheral blood was only 2% of contemporary interballoon concentration, and only 10% of steady-state concentration found during systemic infusion (Jørgensen 1991b). These findings also indicate the safety of SET with respect to the coagulation system. The vast interballoon t-PA concentration was followed by a six times longer elimination rate of t-PA in peripheral blood after SET termination than reported in any other human study on t-PA pharmacokinetics (Jørgensen 1991c). The long half-life of t-PA after SET may be due to t-PA binding to subendothelial tissues exposed to the bloodstream by the deep vessel wall injury enforced by the preceding balloon dilatation (Reilly 1989). Depositing of t-PA, and also of heparin in the vessel wall (Hirsh 1991) provides for sustained fibrinolytic and anti-thrombin activity at dilated sites after SET termination. Prolonged action of other pharmacological agents could most likely be accomplished by their segmental enclosure in blood vessels or body cavities.

Occlusion of the superficial femoral artery by a double-balloon catheter does not lead to peripheral circulatory arrest, but only reduces the average blood flow rate in the calf by 45% during SET (Jørgensen 1991b).

It should be emphasized that agents used for thrombolytic or anti-thrombin treatments are often very expensive. The cost of such treatments could be dramatically reduced by target application of small amounts of agents in relevant arterial segments rather than remote action of large amounts of agents infused into the general circulation.

Besides reducing costs, this approach could also enhance the effect of the agents dramatically due to the very high local concentrations obtained during enclosure, and side-effects reduced.

Apart from rethrombosis, another drawback in endovascular surgery is restenosis which develops weeks to months after balloon dilatation procedures. This phenomenon is due to smooth muscle cell proliferation in the arterial wall which develops in consequence of the deep arterial wall injury enforced by balloon dilatation, but not after simple denuding of the endothelium (Clowes 1991). Restenosis is in part mediated by growth factors secreted from platelets adhering to the injured vessel wall immediately after PTA (Minar 1987). These mitogens induce proliferation and migration of smooth muscle cells into the subendothelium leading to luminal narrowing of the dilated arterial segment, and subsequent hemodynamic failure of the angioplasty procedure. As stated previously, restenosis after femoropopliteal PTA occurs in 30%-50% of cases. In PTCA, the restenosis rate is in the proximity of 40% within 6 months of dilatation (Roubin 1990).

Platelets play an important role for the development of restenosis after balloon angioplasty. A large number of clinical studies have investigated the efficacy of anti-platelet drugs for prevention of restenosis after PTA and PTCA with disappointing results (Minar 1987, Heiss 1987, Cox 1988). Recent experimental studies have indicated that substances such as angiotensin-converting enzyme inhibitors (ACE-inhibitors) and heparin may reduce smooth muscle cell proliferation and migration after balloon angioplasty (Powell 1989, Edelman 1990, Hammerle 1991), but until now, the issue of pharmacological control and prevention of restenosis after balloon angioplasty remains largely unsolved (Clowes 1991). Endovascular stents for mechanical internal support of dilated arterial segments do not prevent restenosis after PTCA and femoropopliteal PTA (Popma 1990, Rousseau 1989).

Human studies on pharmacological agents segmentally enclosed in relevant arterial segments for prevention of late restenosis after balloon angioplasty have never been conducted. However, as indicated, there is strong reason to believe that such approaches would be beneficial for the long-term outcome of balloon angioplasty procedures. Many of the agents previously mentioned could readily be investigated, and many probably adopted, for prevention of both rethrombosis and restenosis after balloon angioplasty procedures.

Introduction of recombinant DNA into endothelium and vascular smooth muscle cells in porcine iliofemoral arteries have been performed using balloon catheters (Nabel 1992). The approach of selective introduction of e.g. growth factor gene products into arterial cells using double-balloon catheters for prevention of restenosis is likely to be used in the future.

A number of balloon catheters have been developed in order to perform segmental treatment of blood vessels. Balloon catheters are described in e.g. US patent specifications Nos. 4 445 892, 4 573 966, 4 610 662, 4 636 195 and 4 824 436, in WO publication No. 91/12846 and DE publication No. 3 227 575.

In principle, the above-mentioned balloon catheters for intravascular use are built in the same way, as they comprise a main catheter body including two spaced balloon elements adapted to be positioned adjacent to, respectively the proximal and the distal ends of the atherosclerotic plaque body of the stenosed or occluded arterial segment, and being expansible against the arterial wall, thus providing a chamber including the relevant arterial segment. The two balloons have a predetermined maximal outer diameter, and between the balloons are one or more orifices in the catheter shaft for injection and removal of the treatment agent. Moreover, in the space between the two balloons there may be placed a third inflatable balloon for vascular dilatation, if not performed with one of the occluding balloons of the double-balloon catheter or with a separate balloon angioplasty catheter.

It should be emphasized that the above-mentioned balloon catheters were designed without recognition of undesired injuring effects of the occlusion balloons to the adjacent vessel wall which undesired effects were originally recognized by the inventor of the present invention in consequence of the novelty of his application of SET in peripheral arteries.

In clinical studies on SET as an adjunct to femoropopliteal PTA, the inventor of the present invention has demonstrated that significant injuries in the arterial

wall may be produced by the two occlusion balloons inflated during SET. On completion arteriograms, visible impressions in the arterial wall, were noted after several treatments. Such impressions denote segments of arterial wall damage, including loss of endothelium and most likely damage to the deeper layers. This unforeseen and inadvertent mechanical side-effect of the occlusion balloons inevitably leads to loss of important anticoagulant properties in the arterial wall. The inadvertently injured arterial segments did not present with significant atherosclerotic disease before SET, and they were not subjected to therapeutic balloon dilatation. On account of the injuries, restenosis of arteries developed at areas which had been exposed only to the occlusion balloons (Jørgensen 1991b).

Subsequently to these clinical findings, experimental studies performed by the inventor of the present invention on post-mortem human femoral arteries, including light microscopy and morphometrical assessment of arterial specimens, showed that a balloon pressure as low as one positive atmosphere during SET may produce splitting of the intima and partial destruction of the internal elastic lamina of the arterial wall (Jørgensen, unpublished data). Balloon pressures of two positive atmospheres often produced deep injuries including medial tears. Balloon pressures within this range are insufficient for therapeutic dilatation of atherosclerotic arterial segments. The balloon pressures recorded during SET, ranging from 0.5 to 1.4 positive atmospheres, were thought to be unharmful (Jørgensen 1991b). It is, however, concluded from the above-mentioned experiments that when SET is performed with double-balloon catheters that are commercially available, there is a substantial risk of inadvertent damage to arterial segments which were not significantly diseased before the treatment. This paradox

that SET may prevent rethrombosis at dilated sites, and at the same time may induce severe damage to non-diseased arterial segments adjacent to dilated sites leading to failure of the treatment due to rethrombosis or restenosis, may well prohibit a widespread use of endovascular segmental pharmacological treatments with double-balloon catheters, unless their construction is improved.

The inventor of the present invention recently reported that rethrombosis after conventional PTA is accompanied by significantly increased levels of cross-linked fibrin degradation products (D-dimer) in peripheral blood (Jørgensen 1992b). Hence, D-dimer may serve as a pre-thrombotic marker in PTA, and could be useful for rapid identification of high-risk patients requiring thrombolytic therapy after PTA for prevention of rethrombosis. The possibility of performing SET in individually selected patients would further encourage radiologists and vascular surgeons to use SET, if appropriate double-balloon catheters were available.

From the results published by the inventor of the present invention, future endovascular surgery is likely to expand through combinations of mechanical revascularization procedures and segmentally enclosed treatments with a variety of pharmacological agents for prevention of subsequent rethrombosis and restenosis. A prerequisite for this trend, however, is development of new balloon catheters specially designed for non-traumatizing segmental occlusion of blood vessels. Fulfillment of this goal would improve the results of PTA and render balloon angioplasty procedures a viable alternative to vascular bypass surgery. In addition, PTA could be offered a large number of patients suffering from relatively mild atherosclerotic disease, whom are not candidates for

vascular bypass surgery.

Any manufacturer of catheters or devices specially designed and equipped to combat rethrombosis and restenosis after balloon angioplasty procedures would thus move into a field of prosperity.

Balloons for angioplasty purposes are made of non-elastic materials and are thus non-compliant in order to provide a balloon force during inflation sufficient to obtain effective vascular dilatation. Therefore, an angioplasty balloon is inflated preferably with fluid from a needle-free syringe which may be specially designed for high-pressure inflation. In the initial phase of balloon inflation, the balloon pressure is near atmospheric. As the balloon volume increases during this phase, the balloon will lay smoothly aside and will respect the uneven outline of the atherosclerotic plaque or stenosis which is intended for dilatation. Once the injected fluid volume equals with the volume of the balloon, continued fluid injection will generate a steep pressure rise in the balloon which will reach the above-mentioned vast balloon pressures. Hereby, the balloon pressure will overcome the forces in the atherosclerotic plaque or stenosis which will deform and fracture. Subsequently under continued fluid injection, the balloon will fully dilate and reach its predetermined maximal outer diameter. During this final phase of angioplasty, the desired luminal expansion of the vessel segment is obtained by deep injuries enforced in the vessel wall. Vessel rupture is avoided because the predetermined maximal outer diameter of the balloon cannot be overcome without bursting the balloon, provided the size of the balloon is correctly chosen.

It is important to realize that once an angioplasty balloon is completely filled with fluid, any further

injection of even a very small fluid volume will produce a vast and uncontrolled pressure rise in the balloon. Therefore, when using known balloon angioplasty catheters for segmental occlusion of e.g. arteries, it is impossible to avoid this pressure rise in the balloon at the time when the balloon occludes the vessel.

The balloons of double-balloon catheters commercially available for SET at present (e.g. TØnnesen™ catheters, Medi-tech) are built as ordinary angioplasty balloons with the above-mentioned features. Therefore, these balloons are oblong and suited for high-pressure inflation with the purpose of deforming and dilating an atherosclerotic arterial segment, leading to a significant risk of inadvertent arterial damage when used for SET.

Another demand to double-balloon catheters used for seclusion of arterial segments is to provide a tight enclosure between the balloons in order to maintain pharmacological agents within the secluded segment. This option can only be achieved if the balloons have full contact with the vessel wall after inflation. The exact inner diameter of a given arterial segment is impossible to assess, as the inner surface of an atherosclerotic artery often is uneven and rugged. Therefore in all cases, a tight enclosure can only be obtained if occlusion balloons have a maximal outer diameter which is slightly larger than the inner diameter of the given vessel.

A number of balloon catheters or devices for inflation of balloon catheters have been developed, by which the inflation pressure of fluid can be adjusted to a predetermined level.

Balloon catheters with inflatable external indicator balloons placed on non-inserted portions of catheters in

order to provide the syringe operator with an additional visual indication of the degree of inflation reached in the ballon are known. Other supplemental visual internal catheter pressure indicia, such as simple pressure gauges have also been utilized, cf. e.g. US patent specifications Nos. 4 723 938, 4 743 230, 5 015 233, 5 019 041 and 5 021 046. However, these and other visually oriented safety devices must be continually watched and attended to by the syringe operator, and probably reacted to, in order to be of any practical value.

Therefore, use of these devices or balloon catheters is difficult and time-consuming since the injected fluid volume usually is very small, and because only a minor surplus of injected fluid will increase the balloon pressure to a level at which the inner wall of the vessel or cavity may be severely injured.

Also particularly in the case of pressure gauges many moving parts are involved which are always subject to malfunction and wear.

US patent specifications Nos. 4 795 431 and 4 865 587 disclose a syringe for inflation of a balloon catheter. The syringe has a volume limiting means, e.g. in the form of an orifice in the wall of the syringe. Moreover, the syringe has a "dead space" which constitutes a pressure absorption zone. This syringe has, however, no pressure limiting effect during fluid injection for inflation of angioplasty balloons, and moreover the "dead space" has to have a very substantial size compared to the volume of the balloon in order to obtain any pressure limiting effect.

WO publication No. 91/05580 describes a device used together with a balloon catheter of the type which has an elastic balloon. Such balloon catheters are used e.g. in

the pulmonary artery for measuring wedge pressures (e.g. Swanz-Ganz catheters) or for removal of acute emboli in the peripheral circulation (e.g. Fogarty catheters), but cannot be used for angioplasty because the maximal pressure obtained in elastic balloons is insufficient to overcome the force in atherosclerotic plaques. On the contrary, these catheters are often moved or withdrawn to larger diameter vessels while the balloon is inflated. The device described in the above-mentioned publication comprises a tubular conduit with a relief aperture extending through the wall thereof, and an inflatable elastomeric sleeve-like safety reservoir member stretched hereabout and sealed to the conduit on both sides of the aperture, constituting a safety balloon. One end of the conduit is adapted to receive fluid from a syringe, and the other end of the conduit is adapted to dispense fluid to the inlet of the balloon channel.

As both the safety balloon and the catheter balloon are of an elastomeric material, they will tend to "pop open" at a particular threshold pressure though the required threshold pressure is slightly higher for the safety balloon than for the catheter balloon. During fluid injection, the catheter balloon "pops open" and the pressure in the catheter balloon keeps increasing until the threshold pressure of the safety balloon is reached, and the safety balloon "pops open" whereby the pressure in the catheter balloon decreases. If fluid injection is continued, the pressure in both balloons will increase. It is obvious that it is impossible to inflate the above balloon catheter to a preferred balloon pressure with any particular great exactitude.

Further, US patent specifications Nos. 3 871 374, 4 116 201 and 4 439 185 describe balloon catheters which are provided with valve means for adjusting the pressure level

in the balloon.

The balloon catheter described in US patent specification No. 3 871 374 is a catheter particularly used for infertilization of females. The exactitude of the closing valve is very poor, since the valve system works by different parts engaging with each other after the predetermined pressure has been attained. One of the engaging parts moves stepwise, and therefore the actual pressure will always be somewhat higher than the predetermined pressure.

Considering the fact that only small volumes of injected fluid can increase the pressure of a very small balloon to a pressure which may be fatal and damaging to a vessel wall, the above-mentioned balloon catheters show no useful solution to this problem.

The balloon catheters described in US patent specifications Nos. 4 116 201 and 4 439 185 are provided with valves normally set open, but which close in response to further fluid injection when the balloon pressure has reached a predetermined level.

The balloon catheter described in US patent specification No. 4 116 201 functions in such a way that the balloon is deflated to a predetermined pressure, once the balloon has been overinflated. This is very inexpedient in terms of segmental arterial enclosure, because even a slightly overinflated balloon may produce fatal injuries in the arterial wall.

The same can be said about the balloon catheter described in US patent specification No. 4 439 185. This balloon catheter is provided with a closing valve represented by a disk which blocks fluid flow when a predetermined pressure

has been reached in the balloon. The amount of fluid which can be injected into the ballon before the valve closes, is highly dependent on the flow under which the fluid is injected into the balloon immediately before the valve closes. When using this catheter, many doctors would be liable to apply extra pressure on the injecting syringe when resistance from the balloon counter-pressure increases in order to ensure that the body cavity is sufficiently closed by the balloon. Consequently in this phase, a surplus of fluid may readily be injected into the balloon, and as previously mentioned, even very small surplus volumes of fluid may increase the balloon pressure to a fatal and damaging level. The closing valve described in US patent specification No. 4 439 185 was suggested as a security means merely to prevent the balloon pressure from getting so high that the balloon would explode whereas the risk of vascular injury during balloon inflation was not considered.

Considering the above-mentioned scientific publication and in particular the studies performed by the inventor of the present invention, it is easy to understand that a balloon catheter with a built-in or remote system which can limit the balloon pressure to a predetermined maximal pressure during inflation, will be considerably useful in the treatment of diseases in hollow tubular organs of any kind in animals and humans, and will be particularly useful in endovascular surgery of such a blood vessel.

By use of such a balloon catheter, segmental arterial seclusion can be performed without a risk of contemporary arterial wall damage. Once this option is achieved, the outer diameter of the occlusion balloons need not be predetermined with great exactitude which, as mentioned before, also is practically impossible, but should rather have a maximal outer diameter slightly larger than the

given vessel.

It is therefore an object of the present invention to provide a balloon catheter with one or more balloons which balloon catheter has been designed in such way that it allows inflation of at least one balloon to a predetermined maximal pressure with a great exactitude without surpassing, at any time, the predetermined pressure by any substantial amount.

Moreover, it is an object of the present invention to provide a device which can be used for inflation of one or more balloons in a balloon catheter of any kind and by means of which device it is possible to inflate one or more balloons to a predetermined maximal pressure with great exactitude without, at any time, surpassing the predetermined pressure with a substantial amount.

The object is achieved by the balloon catheter or the device according to the introductory portion of claim 1 which is characterized by the characterizing portion of claim 1.

With a balloon catheter according to the present invention, or a device according to the present invention connected with any inflatable balloon catheter, it is possible to inflate the balloon or the balloons of the balloon catheter to a predetermined maximal pressure with great exactitude without any risk of overinflating the balloon or the balloons.

The balloon catheter or the device according to the present invention are very simple and easy to handle and require no particular instructions for use. Moreover, when using a balloon catheter or a device according to the present invention, the limitation of the balloon pressure

during fluid injection is achieved by an automatic function of the present invention, and requires no specific interaction or mechanical adjustment or concern for the flow or volume of the injected fluid by the operator of the injection syringe. In this way, the present invention provides a balloon catheter or a device for a balloon catheter which acts in a simple, safe and easy fashion.

When using a balloon catheter or a device according to the present invention, a doctor can easily and with great exactitude inflate one or more balloons of a balloon catheter to a predetermined maximal balloon pressure after the balloon catheter has been introduced into a body cavity and thus avoid any risk of damaging the walls of the body cavity.

According to the present invention, limitation of balloon pressures is achieved by the action of at least one relief valve built into the balloon catheter shaft or assembled in an external device which can be connected with the hubs of a balloon catheter. The relief valve can in principle be of any kind but for purposes of exactitude a valve working by a spring coil is preferred.

The balloon catheter according to the invention can be of any kind, e.g. as described in the above-mentioned publications, wherein a channel containing or connected to a relief valve is connected with at least one inflatable balloon.

The device according to the invention is designed to be connected to balloon catheters of any kind, e.g. as described in the above-mentioned publications.

In a first preferred embodiment of the invention the balloon catheter comprises one inflatable balloon and a fluid channel leading fluid to and from the balloon. The external hub of the channel may be provided with a closing valve which opens by introducing the tip of a syringe. The fluid channel is at some place between the external hub and the balloon provided with a side-branch channel which side-branch channel is provided with a relief valve, preferably a spring coil valve. The spring coil valve is normally closed, but opens when the fluid pressure and thereby the balloon pressure reaches a predetermined level corresponding to the force in the spring coil. The pressure needed to open the valve can be fixed or the spring coil valve can be provided with a regulator means for continuous or stepwise regulation of the opening pressure.

In a second preferred embodiment of the invention the relief valve is a so-called socket valve.

In a third preferred embodiment of the invention the balloon communicates with two channels, one leading fluid into the balloon and one leading fluid out of the balloon.

In a fourth preferred embodiment of the invention the balloon catheter is provided with two or more inflatable balloons, each of which communicate with separate channels leading fluid into and out of the balloons, and furthermore the catheter shaft is provided with one or more channels leading fluid into and out of the compartment secluded between the two balloons.

The balloon catheter or the device according to the present invention can be made of materials which are normally used for making balloon catheters. Such materials are also known from the above-mentioned publications.

Balloons for segmental occlusion of tubular body organs according to the present invention should preferably be made of a non-compliant material as commonly used for high-pressure angioplasty balloons. During inflation, this material will unfold without providing any counter-pressure to the injected fluid until the balloon is completely filled under the given intra-vascular circumstances or the maximal outer balloon diameter is reached. This is contrary to e.g. a latex-balloon, which exerts a substantial counter-pressure until the balloon suddenly pops open. In a latex-balloon the pressure applied on a vessel wall is difficult to estimate. Using a balloon of non-compliant material which furthermore has a maximal outer diameter slightly larger than the diameter of the treated vessel segment, this non-compliant balloon will always obtain full contact with the vessel wall and provide a tight sealing before the balloon has reached its maximal outer diameter. Due to the pressure limiting effect of the present invention incorporated in the balloon catheter or provided by an external device connected to the balloon catheter, vessel wall damage during balloon inflation is prevented. Balloons which are intended for occlusion only should preferably be short or spherical rather than oblong in order to facilitate correct position of the occlusion balloon catheter in all cases. This feature of the balloon is especially mandatory in small calibred arteries and in PTCA. However, the occlusion balloon may also be oblong and thereby suited for high-pressure balloon angioplasty. Subsequently, segmental enclosure can be performed with the same balloon. This feature requires that the pressure limiting action of the present invention incorporated in the balloon catheter or provided by an external device connected to the balloon catheter can be set inactive during high-pressure balloon inflation, which easily can be obtained by e.g. a 3-way stop-cock mounted on the

outlet channels containing the pressure limiting means described in subsequent paragraphs of this publication.

The balloon catheter of the present invention or the balloon catheter with which the device of the present invention can be used, can have different sizes and numbers of balloons. For angioplasty purposes, a double-balloon catheter would be satisfactory in many cases. Such double-balloon catheter could provide high-pressure balloon angioplasty with the distal balloon which then preferably should be oblong, whereafter subsequent segmental enclosure could be obtained with both balloons of the same double-balloon catheter. Concerning balloon angioplasty of small calibred peripheral arteries or in PTCA, a double-balloon catheter intended for segmental occlusion only could be preferred. This catheter should then preferably have two small and spherical balloons in order to obtain correct placement of the balloon catheter in all cases. In such a catheter, high-pressure balloon angioplasty could be accomplished by one of the spherical occlusion balloons or by a third balloon which preferably should be oblong and placed between the two occlusion balloons and preferably provided with a separate injection channel. Hereby segmental enclosure could be undertaken immediately after dilatation without relocation of the catheter.

Although never used in clinical practice, segmentally enclosed pharmacological treatments could probably be useful in inflammatory bowel disease, e.g. Crohn's disease or ulcerative colitis. Balloon catheters suited for this purpose should preferably have large balloons which could have considerable interballoon distance in order to enclose drugs in bowel segments of substantial length. Also in such catheters there could be more than two balloons providing for a number of serial compartments in

order to facilitate drug supply to or flushing of the secluded compartments. Similar multi-balloon catheters could be useful in segmental treatments of other long tubular body organs.

The device according to the present invention could be used for inflation of the balloons in a Sengstaken-Blakemore catheter which is a double-balloon catheter used for hemostasis of bleeding oesophageal varicose veins often associated with cirrhosis of the liver. Using this catheter, it is vital to maintain the pressure of the oesophageal balloon close to approximately 40 millimeters of Mercury. Lower balloon pressures are insufficient for proper compression of the varicose veins whereby bleeding will commence, whereas higher balloon pressures involve a risk of oesophageal rupture which may be fatal. Therefore, pressure reading for proper and safe balloon function including adjustment of the oesophageal balloon pressure of the Sengstaken-Blakemore catheter is usually performed repeatedly during the treatment which is a cumbersome and staff-consuming regimen. Using the device of the present invention, the oesophageal balloon as well as the gastric balloon could easily be inflated to a correct pressure by a stat injection of air or fluid. The injection of air or fluid could be repeated fast and easily as desired, whereas the cumbersome pressure readings could be abandoned.

The present invention will be described in greater detail hereafter with reference to preferred embodiments which are illustrated in the drawings in which:

Fig. 1a is a longitudinal view through a balloon catheter of the present invention where the relief valve is in the closed position.

Fig. 1b shows the relief valve through Fig. 1a in the open position.

Fig. 1c is a longitudinal view through another relief valve provided with a regulator means for regulation of the opening pressure of the relief valve.

Fig. 1d and Fig. 1e are longitudinal views through a third relief valve with exchangeable spring coil elements.

Fig. 2a is a longitudinal view through a second embodiment of a balloon catheter according to the invention.

Fig. 2b is a longitudinal view through a part of the relief valve means of Fig. 2a built together with a syringe means.

Fig. 3a is a longitudinal view of a third embodiment of a balloon catheter according to the invention.

Fig. 3b-3c show different valve means for use in a device connected to or built into a balloon catheter according to the invention.

Fig. 3d is a longitudinal view of an example of a Luer-lock fitting.

Fig. 4 is a longitudinal view of a fourth embodiment of a balloon catheter according to the invention.

The balloon catheter 1 as shown in Fig. 1a consists of a catheter shaft 2 with one inner channel 3 leading to the inner of an inflatable balloon 4. The external hub of the channel 3 may be provided with a closing valve 5 made of

an elastic material such as KRATON® type D or G purchased by Shell Chemical Company. The orifice of the valve 5 is normally closed due to the elasticity of the material, but can be opened by connecting the outlet 6 of a syringe 7 with the valve 5. The syringe 7 is of a conventional type and comprises a house 8, a piston 9, a handle 10, and an outlet 6. The syringe used in connection with a catheter of the kind shown in Fig. 1a can have any other shape provided that it has an outlet 6 that can be connected with the valve 5, e.g. Luer-lock fittings.

The channel 3 has a side-branch channel 11 leading into the inner of a house 12 which is placed at the proximal non-inserted part of the catheter. The house 12 has an outlet channel 13 which may be connected to a not shown collecting means such as a bag or a bowl, which collecting means should have a volume sufficient to collect fluid without causing a pressure increase in the outlet channel 13 or inside the house 12. A spring coil 14 is connected to the inside ceiling 15 of the house 12. In the opposite end of the house 12 the spring coil 14 is connected to a slide member 16 which forms a closure against the floor 17 of the house 12 when the pressure in the balloon 4 and in the channels 3, 11 is below the force in the spring coil 14.

Fig. 1b shows a part of the relief valve of Fig. 1a in the open position. When the pressure in the balloon 4 and the channels 3, 11 becomes higher than the force provided by the spring coil 14 on the slide member 16 the slide member 16 is pressed upwards, and fluid passes through the channel 11 into the inside of the house 12 and through the outlet channel 13.

Fig. 1c shows a variant relief valve of the preferred embodiment of Fig. 1a. The channel 3 in the catheter shaft

2 leads fluid to and from the balloon 4 as illustrated in Fig. 1a. The side-branch channel 11, the outlet channel 13, the spring coil 14, and the slide member 16 are equal to the parts in Fig. 1a. The house containing the spring coil 14 and the slide member 16 consists of the floor 17, the walls 18, and a movable ceiling 19. The ceiling 19 is connected to a regulator means 20 which has a thread 21 fitting into a thread 22 on the inside walls 18 of the house. By rotating the regulator means 20 the ceiling 19 can be moved up and down and thereby regulating the force by which the spring 14 presses the slide member 16 against the floor 17. Hence, by rotating the regulator means 20 the opening pressure of the relief valve can be regulated. A balloon catheter of the invention with a relief valve as illustrated in Fig. 1c is preferably also provided with an indicator means indicating the pressure in the balloon 4 and the channels 3, 11. Such a pressure indicator means can be of any kind, e.g. those described in the above-mentioned publications.

Fig. 1d shows another variant of the relief valve of the preferred embodiment of Fig. 1a. The reference numerals 2, 3, 11, 13, 14, 16, and 17 denote parts corresponding to the same numerals in Fig. 1a and Fig. 1c. The house 26 containing the spring coil 14 and the slide member 16 is separated in two parts. The lower part of the house has the walls 23 fitted with outer threads 24. The upper part of the house has the walls 28 and a ceiling 27, and is equipped with the outlet channel 13. The lower part of the upper walls 28 is provided with an inner thread 25 fitting into the thread 24 on the outer side of the lower walls 23, whereby the two parts of the house can be tightly assembled. The spring coil 14 carrying the slide member 16 can be mounted to the inside ceiling 27 of the house or, as a separate spring coil element, can be placed there before assembly of the two parts of the house. Hereby, the

spring coil 14 and the slide member 16 can be exchanged, thus providing different spring forces and ability for stepwise regulation of the opening pressure of the relief valve system during operation of the balloon catheter. The channel 3 or the channel 11 or the lower part of the house 12 should preferably be fitted with a stop valve or fluid lock in order to prevent loss of balloon fluid pressure during dispersion of the house 26, while performed during operation of the balloon catheter.

Fig. 1e shows a separate spring coil element consisting of a spring coil 14 and a slide member 16. The spring coil element shown in Fig. 1e also contains a protective spring coil house consisting of the walls 29 and the ceiling 30. The spring coil 14 is fixed to the inside of the ceiling 30. The spring coil element can be used in a relief valve part as the one shown in Fig. 1d by bringing the ceiling 30 into contact with the inside of the ceiling 27, whereafter the house can be assembled. Exchangeable spring coil elements can preferably be offered for sale in boxes containing an appropriate selection of spring coil elements with different predetermined spring forces for use in different types of balloon catheters according to the present invention or in a device according to the present invention.

Fig. 2a is a cross-sectional view of a conventional catheter 100, a device according to the present invention 110 and a conventional syringe 107. The balloon catheter 100 consists of a catheter shaft 102 with a channel 103, providing a passageway between the inflatable balloon 104 and the external hub which may be provided with a closing valve 105 of the same type as the closing valve 5 of Fig. 1a. The syringe 107 can be of a conventional type and comprises a house 108, a piston 109, an outlet 106, and a not shown handle.

The device 110 of the invention comprises a tube 111 with a channel 112 which is in connection with e.g. four side-branch channels 113, 114, 115, 116 running through the wall of the tube 111. The three distal side-branch channels 113, 114, 115 are each covered with a socket 117, 118, 119 which are made of an elastic material such as polyurethane, silicone or polyethylene. The sockets 117, 118, 119 surround the tube 111 and are kept in place by the elastic forces of the material. The elastic force of the sockets 117, 118, 119 against the openings of the side-branch channels 113, 114, 115 is predetermined by the tensile force obtained during manufacturing of the socket material, and differ as the socket 117 has the highest force and the socket 119 has the lowest force. The tube 111 is surrounded by a sliding socket 120 resting on elastic sealing rings 123, 124 which provide a tight seal between the socket 120 and the tube 111. Hereby, a closed chamber is formed inside the socket 120 which chamber contains part of the tube 111. The socket 120 can slide longitudinally on the tube 111 and thereby obtain 5 different positions, as in this example.

In order to facilitate a smooth sliding function of the socket 120 and to diminish wear of the sockets 117, 118, 119 during operation of the device 110, the sockets 117, 118, 119 and the sealing ring 124 may preferably be placed in furrows or ditches engraved in the outside wall of the tube 111 corresponding to the position of the side-branch channels 113, 114, 115 whereby the outer surface of the sockets 117, 118, 119 and the sealing ring 124 become nearly or completely aligned with the outer aspect of the tube 111. Additional sealing rings similar to the sealing ring 124 may be placed at each side of the sockets 117, 118, 119 and the side-branch channel 116.

In the first position, the socket 120 is slided distally and covers all of the sockets 117, 118, and 119 as well as the opening of the side-branch channel 116. In the second, third and fourth position the socket 120 is stepwise slided proximally, and successively uncovers the sockets 117, 118, 119. In the fifth position, the socket 120 is fully retracted, whereby also the opening of the side-branch channel 116 is uncovered. The channel 112 passes axially through the device 110 and runs between an inlet with a closing valve 121 and an outlet 122 which outlet fits with the bub of a balloon catheter. The closing valve 121 is of the same kind as the closing valve 5 described and shown in Fig. 1a.

In use the device 110 is connected with a balloon catheter 100 and with a syringe 107 filled with a fluid or air as shown in Fig. 2a. When the socket 120 is in the first position, it covers all sockets 117, 118, 119 and the side-branch channel 116. In this position, the device 110 provides no pressure relief but serves merely as a connecting tube, and high-pressure balloon inflation may be obtained by fluid injected with the syringe 107. Moving the socket 120 to its second position will uncover the socket 117. Hereby, the fluid pressure in the balloon 104 will instantly be maximized according to predetermined tensile force provided by the socket 117 against the external wall of the tube 111. If high-pressure balloon inflation was applied prior to retraction of the socket 120, surplus of fluid will escape through the side-branch channel 113 and the pressure in the balloon 104 will decline accordingly. If fluid is injected from the syringe 107, the balloon 104 will inflate until the balloon pressure equals with the pressure determined by the tensile force in the socket 113 against the external wall of the tube 111. Additional fluid injected through the channel 112 of the device 110 will thereby escape through

the side-branch channel 113.

Likewise, when the socket 120 is retracted to its third and fourth position, the sockets 118, 119 are exposed and fluid may escape through the side-branch channels 114, 115. As the tensile force of the elastic socket material declines through sockets 117, 118 and 119, the pressure in the balloon 104 will gradually decline according to the extent of retraction of the socket 120. When the socket 120 is fully retracted to its fifth position, the side-branch channel 116 is also uncovered, allowing unlimited escape of fluid and collapse of the balloon 104.

In a not shown particularly preferred variant of the embodiment of the device 110 of the present invention, the tubular socket 120 can rotate rather than slide over the elastic sockets 117, 118, 119 and the side-branch channel 116 of Fig. 2a. The elastic sockets 117, 118, 119 are manufactured in the same way as described above, whereas the rotating socket 120 rests on two elastic sealing rings 123, 124, preferably solid O-rings which provide a tight seal between the socket 120 and the tube 111. The O-rings fit into circular grooves which are carved in each end of the inner aspect of the socket 120 in order to keep the socket 120 in place and prevent it from sliding when it is rotated e.g. between the thumb and the index finger. Hereby, a closed chamber is formed inside the socket 120 which chamber will receive any fluid which may drain from the side-branch channels 113-116 during balloon inflation. Preferably, the socket 120 covers all of the tube 111. For fluid outlet from the chamber, the socket 120 is equipped with a recess or an outlet channel which may lead to a fluid collection bag. A part of the inside aspect of the socket 120 is carved, providing the above-mentioned circular grooves as well as four furrows or ditches at positions corresponding to the elastic sockets 117, 118,

119 and the side-branch channel 116. The furrows or ditches should be semi-secular and may take up to about half of the inner aspect of the socket 120, whereas the remaining part of the inner aspect of the socket 120 in uncarved and is thus in close contact with the tube 111 or the suckets 117-119. The most distal furrow or ditch corresponding to the socket 117 is the longest, and the most proximal furrow or ditch corresponding to the side-branch channel 116 is the shortest. Because the furrows or ditches are carved stairwise as described, a stepwise pressure regulatory effect of the socket 120 on the balloon 104 is obtained by rotating the socket 120 clockwise. Hereby, the most distal furrow or ditch will first uncover the socket 117 which thereby will provide pressure limitation in the balloon 104 in the same manner as described above corresponding to the second position of the sliding socket embodiment. By rotating the socket 120 further clockwise, the second and subsequently the third furrow or ditch in the stairwise row will uncover the sockets 118 and 119, respectively, which sockets 118, 119 will provide for further fluid outlet and pressure reduction in the balloon 104. By rotating the socket 120 to its upmost clockwise position, the side-branch channel 116 will be uncovered and provide for unlimited fluid escape and collapse of the balloon 104.

This embodiment of the present invention is especially suited for construction together with a balloon catheter, as the tube 111, including the elastic sockets 117, 118, 119 as well as the side-branch channel 116, can be a part of the catheter shaft as indicated in Fig. 2e, and the rotating socket 120 can be a tube means fitting on the outside of the catheter shaft. In terms of mounting this embodiment on a catheter shaft, the socket 120 may preferably be in two parts which interphase at a fluid-tight circular connection. The distal portion of this

socket 120 is the rotating part, containing the above-mentioned furrows or ditches as well as a distal groove fitting with an O-ring, whereas the proximal part of the socket 120 is fixed to the catheter shaft by means of cast rigdes or alike fittings and is provided with a recess or an outlet channel intended for disposal of fluid escaping from the side-branch channels 113-116. The inner aspect of the rotating part of the socket 120 and the external wall of the catheter shaft may contain interdigitating notches which prevent rotation of the socket 120 beyond its range of proper action. Furthermore, the rotating part of the socket 120 may on its outer aspect be provided with engraved dots or figures indicating the actual pressure relief provided at any time by this embodiment of the invention at any of the stepwise positions of the rotating part of the socket 120. These dots or figures may be read relative to an engravement on the catheter shaft just distal to rotating part of the socket 120.

Using this preferably preferred-embodiment of the invention, the operator can perform high-pressure balloon angioplasty by first rotating the socket 120 to its upmost counterclockwise position, providing occlusion of all side-branch channels 113-116 running through the catheter shaft, and secondly inflate the distal balloon of a double-balloon catheter with fluid injected through channel 103, 112. When angioplasty is completed, the socket 120 can be rotated to its far clockwise position, whereby the side-branch channel 116 will be exposed, providing collapse of the balloon 104. Immediately thereafter, and with a minimum attention or concern by the operator in terms of balloon conditions, the balloon catheter can readily be relocated and the two balloons positioned at each end of the just dilated segment. Optionally, the operator may choose to fully deflate the distal balloon with a syringe before relocating the

catheter. The socket 120 is then quickly and easily rotated counterclockwise until the engraved dot or figure on the socket 120 indicates that all side-branch channels expect side-branch channel 113, corresponding to the elastic socket 117, are covered by the socket 120. Optionally, any other position of the socket 120 can be cosen as appropriate. Immediately after, the operator can inject any volume of fluid through the channel 103, 112 leading to the balloons, which balloons will inflate and obtain a pressure equal to the tensile force in the elastic socket 117 or in any other socket chosen to be active during inflation. Surplus of injected fluid will pass through the outlet in the socket 120. In this way, the operator can perform both balloon angioplasty and subsequent segmental enclosure of blood vessels with the upmost comfort and absense of concern for inadvertant vessel wall damage during balloon inflation.

In everyday clinical practice, an embodiment of the present invention with one or two elastic sockets for balloon pressure limitation as well as a side-branch 116 for balloon collapse may be satisfactory for performing high pressure balloon angioplasty and subsequently segmentally enclosed pharmacological treatment of blood vessels.

By using the device 110 of Fig. 2a or the variant of the device 110 as described above, the operator can choose between e.g. three different pre-set pressures for balloon inflation as well as high-pressure balloon inflation and instant balloon collapse. For easy handling, the sliding or rotating socket 120 may preferably have a ribbed or carved outer surface. The socket 120 may also be provided with a recess or an outlet for collection of escaping fluid. The device 110 may be manufactured in variants with different predetermined socket forces appropriate for use

in different types of balloon catheters.

Fig. 2b illustrates the device 110 of Fig. 2a built together with the syringe 107. The same reference numerals are used to denote corresponding parts. It is obvious that the device 110 of Fig. 2a also can be built into the shaft of a balloon angioplasty catheter.

Fig. 3a shows a third type of catheter of the invention. The catheter tube 202 comprises two channels 201, 203 providing inlet and outlet, as indicated by directional arrows, of fluid to an inflatable balloon 204. Inside each of the channels 201, 203 is a valve 205, 206 consisting of a spring coil 207, 208 and a valve ball 213, 214 fixed between a lip or a flange 209, 210 and a flange or an O-ring 211, 212. The valves 205, 206 are in principal equal although their purposes and functions are different. The force of the spring 208 in the valve 206 is low, because the valve 206 is constructed to prevent backflow of fluid during injection through the inlet channel 203. During fluid injection through channel 203, the ball 214 and the spring 208 are depressed without any particular resistance to the injection force and fluid is conveyed to the balloon 204. As soon as fluid injection is halted the spring 208 unfolds and presses the ball 214 against the flange or O-ring 212, thus preventing backflow of fluid and loss of fluid pressure from the balloon. During inflation of the balloon 204, the channel 202 fills with injected fluid, but the valve 205 will remain closed until the fluid pressure and thus the pressure in the balloon 204 reaches a level equal to the pressure force of the spring coil 207. Additional fluid injection will subdue the force in the spring coil 207 which will open as the valve ball 213 will be depressed from the flange or O-ring 211. Additional fluid will thereby pass out of the catheter shaft through the outlet channel 201. The

external hub of the outlet channel 201 may be connected with a collection means as described in connection with Fig. 1a. The balloon 204 can be fully deflated by applying negative pressure with a syringe connected to the hub of the outlet channel 201, whereby both spring coil valves 206, 205 will open and all fluid will be removed from the balloon 204.

A relief valve means such as described in fig. 3a may easily be built into a balloon catheter shaft, as the spring coil valves are placed longitudinally inside the channels. A relief valve means such as described in Fig. 3a may also be manufactured as a separate device which can be provided with exchangeable spring coil elements as described in connection with Figs. 1d-1e. A relief valve means such as described in Fig. 3a provides a highly sensitive pressure regulator means by which the maximal balloon pressure is determined by the pre-set force in the spring 207.

Fig. 3b is a variant of the catheter shown in Fig. 3a. The same reference numerals are used to denote corresponding parts. The catheter shaft 202 contains separate inlet and outlet channels 203, 201 which exit the catheter shaft as separate tubes 202b, 202a. A spring coil valve 205, corresponding in construction and function to the spring coil valve 205 in Fig. 3a, is placed longitudinally inside the outlet channel 201 in its course through the tube 202a. The free end of the tube 202a should preferably be specially marked or colored in order to warn against erroneous fluid injection through the outlet channel 201. The free end of the tube 202b containing the inlet channel 203 is in this example provided with a closing valve 215 of the same type as the closing valve 5 described and shown in Fig. 1a.

Fig. 3c shows a device according to the invention to be used in connection with a balloon catheter 216 with separate inlet and outlet channels 203, 201. The inlet channel 203 is provided with a closing valve 215 corresponding to the valve 215 of Fig. 3b. The device 220 consists of a tube 221 containing a channel 222. A spring coil valve 205 of the same kind as the valve 205 of Fig. 3a is placed longitudinally inside the channel 222. The device 220 has a cone tip 224 which fits into the hub of the outlet channel 201, which may contain a closing valve 223. The connection may be provided by a standard threaded Luer-lock as shown in Fig. 3d. A selection of devices 220 can have fixed spring coil valves 205 with appropriate spring forces for use with different types of balloon catheters or the device 220 may be provided with exchangeable spring coil elements as described in connection with Figs. 1d-1e. The device 220 may also be designed with two or more parallel pairs of channels among which the outlet channels each contain a fixed or exchangeable spring coil valve for pressure limitation in multi-balloon catheters. The tube 221 of the device 220 can preferably lead to a fluid collection means as described in Fig. 1a.

Fig. 3d shows a Luer-lock fitting which can be used for connecting a syringe to a balloon catheter or a device according to the invention and particularly for connecting to a device according to the present invention to a balloon catheter.

The Luer-lock comprises two parts, a male part 237 and a female part 236. The male part 237 is provided with a cone tip 224a of the device. The reference numerals 221a and 222a denote parts corresponding to the reference numerals 221 and 222, respectively, of Fig. 3c. The cone tip 224a is surrounded by a rotatable socket 234 which has a flange

233 fitting into a groove 232. The flange 233 is the only part of the male part 237 which is in contact with the cone tip 224a. The inside wall of the socket 234 is provided with a thread 235.

The female part 236 is provided with a free end of a tube 216a of a not shown balloon catheter. The free end of the tube 216a contains a channel 201a for passage of fluid into or out of the balloon or balloons. The female part 236 contains a wall 230 which is provided with an extension of the wall of the tube 216a. At the free end of the wall 230 is a flange 231, which flange fits into the thread 235 of the male part 232. The female part preferably also contains a longitudinal flange 238.

By placing the female part 236 against the male part 237 in such a way that the core tip 224a fits into the channel 201a and thereafter rotating the socket 234, the flange 231 is assembled with the thread 235 and a fluid tight connection is obtained.

Fig. 4 shows a particularly preferred embodiment of a catheter of the invention. The catheter comprises a catheter shaft 302 mounted with two balloons 304, 306. An inlet channel 303 runs along the shaft 302 from an inlet hub 321 and communicates with each of the ballons 304, 306. The inlet channel 303 may have a closing valve 316 near its hub 321 and may have a backflow preventive spring coil valve placed inside the channel, corresponding in construction and function to the spring coil valve 206 in Fig. 3a. An outlet channel 301 is also connected with each of the balloons 304, 306 and runs along the catheter shaft 302, thus providing fluid outlet from the balloons 304, 306 to a collecting bag 308 which may be attached to the catheter shaft or may be remotely placed. Longitudinally in the outlet channel 301 is placed a spring coil valve

305, corresponding in construction and function to the spring coil valve 205 in Fig. 3a. A third channel 310 serves as an infusion channel for e.g. drug solutions and runs from an inlet hub 320 mounted with a closing valve 315 to an outlet 312 between the two balloons 304, 306. A fourth channel 309 serves as an outlet channel for drug solutions and runs from an opening 311 between the balloons 304, 306 to a connection point with the balloon outlet channel 301 in a part of the catheter shaft proximal to the balloons 304, 306. The spring coil valve 305 is placed proximal to the point of connection between the channels 309 and 301. The drug solution outlet channel 309 is furthermore provided with a spring coil valve 307 for preventing backflow of fluid into the compartment between the balloons 304, 306. The valve 307 corresponds in construction and function to the spring coil valve 206 in Fig. 3a. The closing valves 315, 316 are of the same kind as the valve 5 described and shown in Fig. 1a.

The catheter of Fig. 4 is preferably used for segmental pharmacological treatment of secluded vascular segments, e.g. segmentally enclosed thrombolysis after PTA or segmentally enclosed anti-platelet therapy after PTCA.

In use the double-balloon catheter of Fig. 4 is guided into an artery by means of a guide-wire or a guiding catheter and under fluoroscopic observation. The catheter is placed with the balloon 304 distal to and the balloon 306 proximal to the vascular segment intended for enclosed pharmacological treatment. As fluid is injected into the balloon inlet channel 303 and gradually fills the balloons 304, 306 and the balloon outlet channel 301, the valve 305 remains in the closed position. During balloon inflation, flow of fluid from channel 301 through channel 309 into the compartment between the balloons 304, 306 is prevented by the valve 307. When the balloons 304, 306 are inflated

to a predetermined pressure level defined by the force of the spring in the valve 305, this valve opens and fluid passes through the channel 301 and into the collecting bag 308 if fluid injection is continued. The collecting bag is preferably transparent for the operator to see when the predetermined pressure is reached. When the balloons are properly inflated the operator may inject or infuse a drug solution for treatment of the secluded arterial segment between the balloons 304, 306 into the channel 310. As the interballoon compartment gradually fills with the drug solution, escape of drug solution through channel 309 is prevented by the spring coil valve 305 which is closed. The backflow preventing valve 307 provides no significant resistance to outlet of drug solution through channel 309. When drug infusion is continued, the interballoon pressure of the drug solution may gradually increase and eventually reach a pressure equal to the pressure in the balloons 304, 306. At this point, the spring coil valve 305 will open and allow surplus of drug solution to escape through the outlet channel 309 to the collecting bag 308. Because the valve 305 controls both the interballoon compartment pressure as well as the balloon pressure, and because the balloon and the drug solution outlet channels 301, 309 are connected distal to the valve 305, outlet of drug solution will not lead to a loss of balloon pressure during this phase. Backflow of drug solution and balloon fluid into the secluded vessel compartment is prevented by the valve 307.

Using a double-balloon catheter of Fig. 4 for segmental pharmacological treatment of blood vessels, infused drug solutions will not escape beyond the balloons and into the general circulation because the drug solution pressure will stay at or below the balloon pressure. In addition, the separate inlet and outlet channels for drug solutions allows continuous flushing of a secluded vessel segment,

whereby the concentration of a drug solution can be maintained at its maximum during this treatment. In order to facilitate flushing of the secluded compartment, the openings 311, 312 are preferably located at each end of the interballoon part of the catheter shaft. By providing the non-inserted part of the catheter shaft with a side-branch channel connecting with the drug outlet channel 309 distal to the spring coil valve 307, and providing this side-branch channel with a house as described in Fig. 1c, but without a spring coil valve, the regulator means of the house described in Fig. 1c may serve as a manual vent for unlimited outlet of drug solution in cases where continuous segmental flushing of the interballoon compartment is desired.

This flushing facility of the catheter could also be used to rinse vessel segments for blood, allowing the catheter to be adopted for use together with e.g. angioscopy, which requires a blood-free visual field near the scope tip to provide for proper visualization of the interior of a vessel. The balloons may be fully deflated by applying negative pressure with a syringe connected to the hub of the outlet channel 303 or by applying negative pressure in the collection means 308.

A balloon catheter as described in Fig. 4 will provide a pressure regulation of both the balloon and the interballoon pressures which is similarly sensitive as the regulation obtained with the catheter shown in Fig. 3a.

A number of different balloon catheters and devices suited for low-pressure balloon inflation and segmental pharmacological treatment of blood vessels and other tubular body organs of different size and location can be manufactured through combinations of the above-mentioned pressure limiting and regulatory means. In addition,

balloon catheters according to the present invention preferably should have lumens for passage of guide-wires or positioning helping means.

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Patent Claims:

1. A balloon catheter comprising at least one inflatable balloon and a fluid inlet for injecting fluid into the balloon (4, 204, 304, 306) or a device adapted to be connected to a balloon catheter with at least one inflatable balloon (104) and a fluid inlet for injecting fluid into the balloon which device has at least one channel (112, 222) for fluid which channel, when connected to a balloon catheter is in communication with the inlet or an outlet from the balloon catheter,

CHARACTERIZED in that

the balloon catheter or the device comprises a relief or by-pass valve means (205, 305) placed in or in connection with a channel (3, 103, 112, 201, 301) for fluid, which relief or by-pass valve means normally is closed, but open when the balloon pressure reaches a predetermined level, so that further injected fluid can escape through the relief or by-pass valve.

2. A balloon catheter or a device according to claim 1, CHARACTERIZED in that the relief or by-pass valve means is placed in a channel or in connection with a channel (3, 103, 112) for the passage of fluid into the balloon or balloons.

3. A balloon catheter or a device according to claim 1, CHARACTERIZED in that the relieve or by-pass valve means (205, 305) is placed in a channel or in connection with a channel (201, 301) for the passage of fluid from the balloon or balloons.

4. A balloon catheter or a device according to claims 1-3, CHARACTERIZED in that the relief or by-pass valve (205, 305) is placed in a channel (201, 301) for the passage of fluid into or from the balloon or balloons.

5. A balloon catheter or a device according to claims 1-3, CHARACTERIZED in that the relief or by-pass valve is placed in connection with a channel (3, 103, 112) for the passage of fluid into or from the balloon or balloons.

6. A balloon catheter or a device according to claims 1-5, CHARACTERIZED in that the relief or by-pass valve means (205, 305) is a spring coil valve and comprises a spring coil (14, 207) and a slidemember or a valve ball (16, 213), which slidemember or valve ball is connected to or in contact with one of the ends of the spring coil (14, 207) and is pressed against a floor, flange or O-ring (17, 211) while the pressure in the balloon or balloons (4, 204, 304, 306) is lower than the predetermined level of pressure.

7. A balloon catheter or a device according to claim 4, CHARACTERIZED in that the relief or by-pass valve (205, 305) is a spring coil valve and comprises a spring coil (207) with a first and a second end where the first end is connected to or in contact with a flange or O-ring (211) while the pressure in the balloon or balloons (204, 304, 306) is lower than the predetermined level of pressure.

8. A balloon catheter or a device according to claim 5, CHARACTERIZED in that the relief or by-pass valve is built into a house (12, 26) with an outlet channel (13) and that a channel (11) provide a passage for fluid from the channel (3, 103, 112) into the house while the relief or by-pass valve is opened.

9. A balloon catheter or a device according to claim 8, CHARACTERIZED in that the house (12, 26) contains a spring coil 14 with a first and a second end where the first end is connected to or in contact with the ceiling (15, 19, 27) of the house and the second end is in contact or connected to a slidemember or valve ball (16) which slidemember or valve ball is pressed against the floor (17) of the house and thereby close the outlet of the channel (11) while the pressure in the balloon or balloons (4) lower than the predetermined level of pressure.

10. A balloon catheter or a device according to claim 9, CHARACTERIZED in that the ceiling (19) of the house is movable and can be moved by rotating a regulator means 20 which has a thread (21) fitting into a thread (22) on the inside walls (18) of the house.

11. A balloon catheter or a device according to claims 6, 7, 9 and 10, CHARACTERIZED in that the spring coil (14, 207) or the spring coil (14, 207) and the slidemember or valve ball (16, 213) are exchangeable.

12. A balloon catheter or a device according to claim 11, CHARACTERIZED in that the house (26), the device or the catheter containing the relief or by-pass valve is made in two separable parts which are thightly assembled to each other, preferably by a thread connection and that the spring coil (14) or the spring coil (14) and the slide-member or valve ball (16) can be exchanged by separating the two parts.

13. A balloon catheter or a device according to claim 5, CHARACTERIZED in that the relief or by-pass valve comprises a channel (113, 114, 115) providing a passage for fluid from the channel (103, 112) to an outlet through the tube wall and which outlet is covered by a socket

(117, 118, 119) of an elastic material which socket is kept in place by the elastic force of the material wherefrom fluid can escape through the channel (113, 114, 115) when the pressure in the balloon or the balloons (104) reaches a pressure that results in a force against the inside of the socket (117, 118, 119) that surpasses the tensile force provided by the socket (117, 118, 119) against the external wall of the tube (111).

14. A balloon catheter or a device according to claim 13, CHARACTERIZED in that the balloon catheter or device comprises two or more relief or by-pass valves each comprising a channel (113, 114, 115) and a socket (117, 118, 119) and that the sockets (117, 118, 119) provide different tensile forces against the external wall of the tube (111) and, when the valves are out of function, is covered by a slidable or rotatable socket (120) which socket (120) rests on sealing rings (123, 124).

15. A balloon catheter or a device according to claim 14, CHARACTERIZED in that the internal wall of the socket 120, when the valve is inactive, is in close contact with the external side of the sockets (117, 118, 119).

16. A balloon catheter or a device according to claim 15, CHARACTERIZED in that the socket (120) is slidable and that one or more of the sockets (117, 118, 119) can be uncovered by sliding the socket (120) and that the sockets 117, 118, 119 are uncovered in decreasing order according to the tensile forces provided against the external wall of the tube (111).

17. A balloon catheter or a device according to claim 15, CHARACTERIZED in that the socket (120) is rotable and that the internal wall of the socket (120) is provided with a number of semi-circular furrows or ditches, which

in number are equal to the number of sockets (113, 114, 115) and which furrows or ditches have different lengths and correspond to the sockets and the greater the force provided by a socket (113, 114, 115) against the external wall of the tube (111) the longer the furrow or the ditch corresponding is, and that the socket (120) is provided with an outlet channel and that one or more channels or the like provides passages for fluid from the furrows or ditches to the outlet channel.

18. A balloon catheter or a device according to claims 1-17, CHARACTERIZED in that the outlet tube or channel (13, 201, 222, 301) is connected to an unpressurized collecting means (308) which is attached to catheter or device or is remotely placed.

19. A balloon catheter or a device according to claims 1-18, CHARACTERIZED in that the catheter or device also comprises a manually operable valve with an open and closed position which valve in its open position provides a vent for unlimited escape of fluid.

20. A balloon catheter or a device according to claims 1-19, CHARACTERIZED in that the balloon or balloons are of a non-compliant material.

21. A balloon catheter or a device according to claims 1-20, CHARACTERIZED in that the catheter comprises one balloon (4, 104, 204).

22. A balloon catheter or a device according to claims 1-20, CHARACTERIZED in that the catheter comprises two or more balloons (304, 306).

23. A balloon catheter or a device according to claim 22, CHARACTERIZED in that the catheter comprises two balloons

(304, 306) placed with a distance.

24. A balloon catheter or a device according to claim 23, CHARACTERIZED in that the two balloons (304, 306) are small and spherical or that one of the balloon is small and spherical and the other balloon is oblong.

25. A balloon catheter or a device according to claim 22, CHARACTERIZED in that the balloon comprises three balloons placed with a distance.

26. A balloon catheter or a device according to claim 25, CHARACTERIZED in that the distal and the proximal balloons are small and spherical.

27. A balloon catheter or a device according to claims 22-26, CHARACTERIZED in that one channel (303) provides a passage for fluid into both of the balloons (304, 306) or into the distal and the proximal balloons and that another channel (301) provides a passage for fluid out of both of the balloons (304, 306) or out of the distal and the proximal balloons and that the channel (301) contains or is connected to a relief or by-pass valve (305).

28. A balloon cathether or device according to claims 22-27, CHARACTERIZED in that the catheter comprises one or more channels (309, 310), preferably two channels, which channel or channels provide passage for fluid into and out of the space between two balloons (304, 306).

29. A balloon catheter or device according to claim 28, CHARACTERIZED, in that the passage for fluid into and out of the space between the two balloons is provided with an inlet channel (310) and an outlet channel (309), respectively, which outlet channel is provided with a valve preventing backflow and that one of the channels

(309, 310) contains or is connected to a relief or by-pass valve.

30. A balloon catheter or device according to claim 29, CHARACTERIZED in that the outlet channel (309) is connected to the outlet channel (301) and that the relief or by-pass valve is placed in the resulting channel.

31. A device according to claims 1-30, CHARACTERIZED in that the device contains a male part (237) of a Luer-lock and that the catheter contains a female part (236) of a Luer-lock.

32. A balloon catheter according to claims 1-30, CHARACTERIZED in that it also contains a lumen for passage of a guidewire or a positioning helping means.

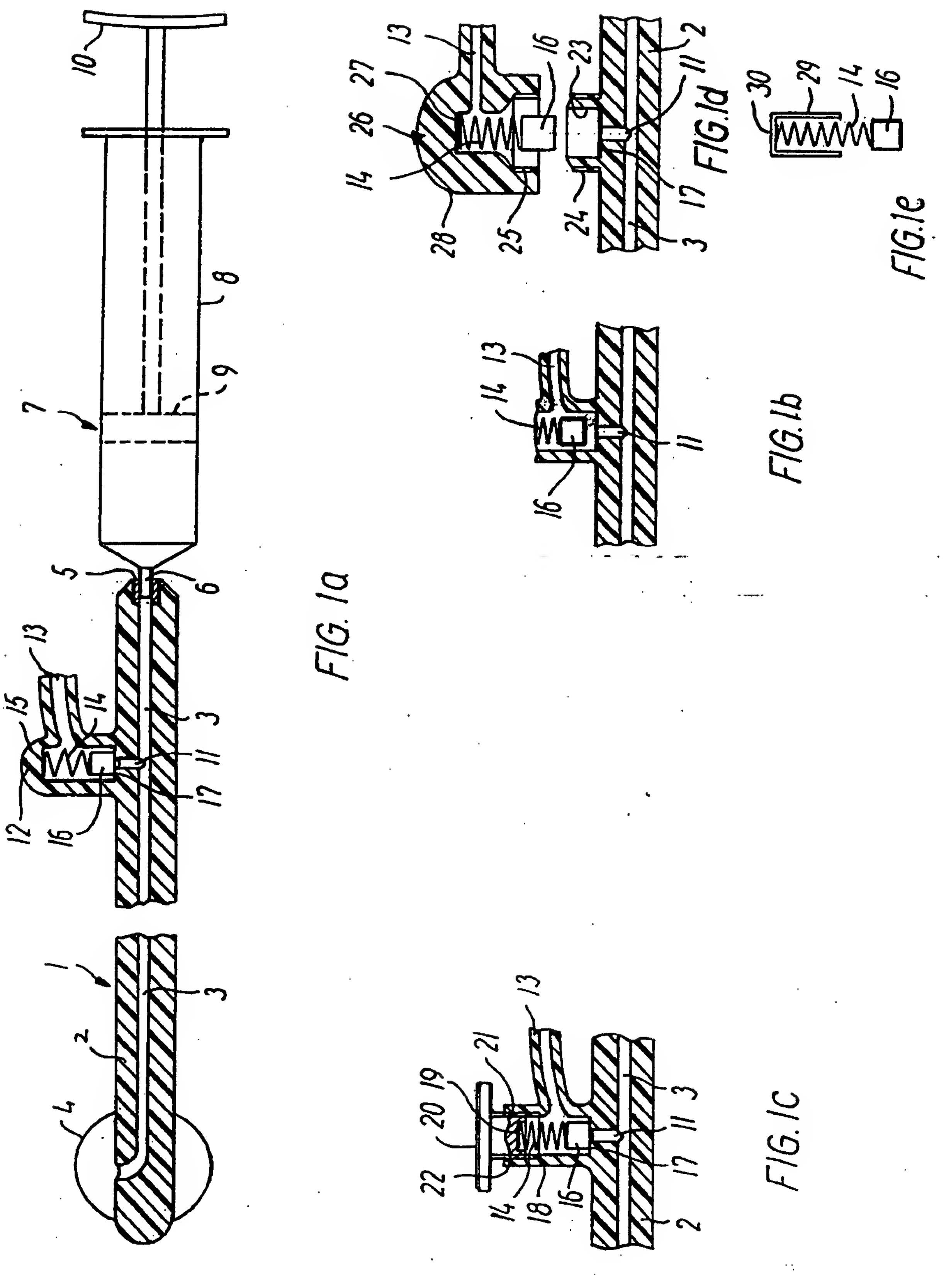

FIG. 1a

FIG. 1b

FIG. 1c

FIG. 1d

FIG. 1e

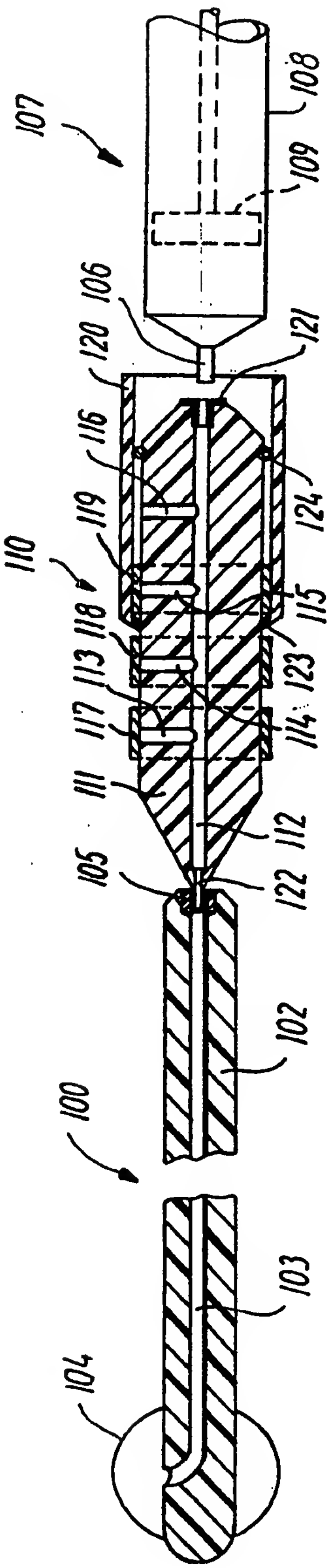
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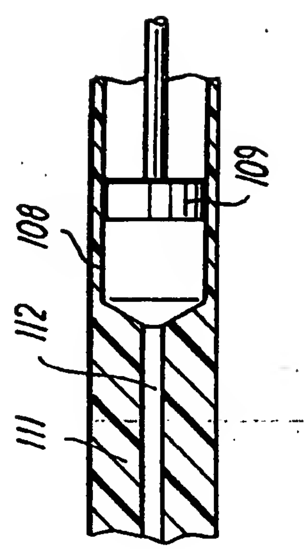
FIG. 2a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111

FIG. 2b

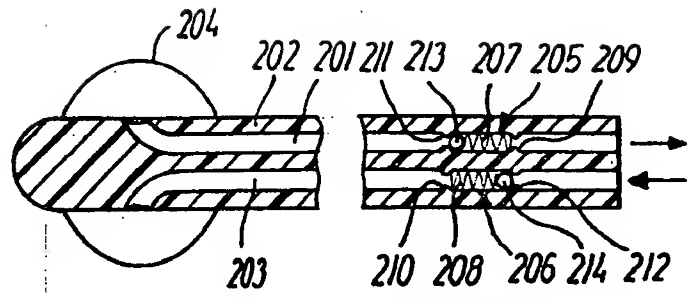

FIG.3a

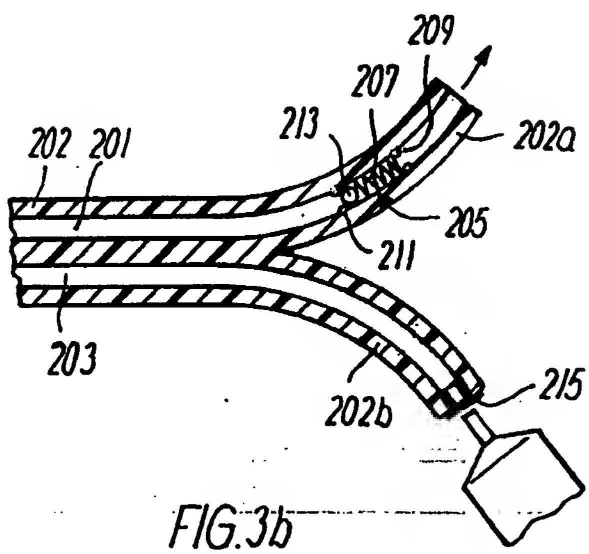

FIG.3b

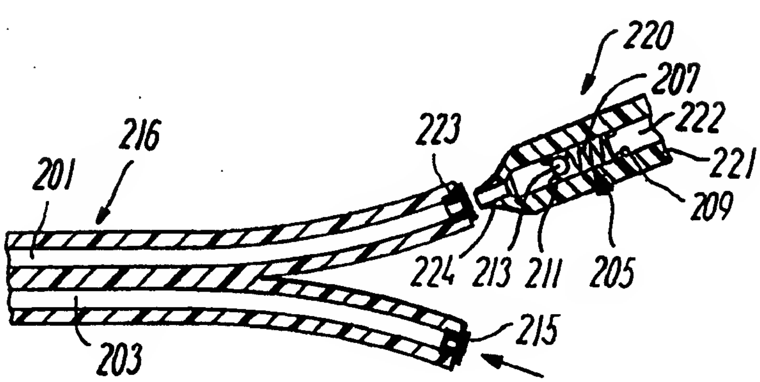

FIG.3c

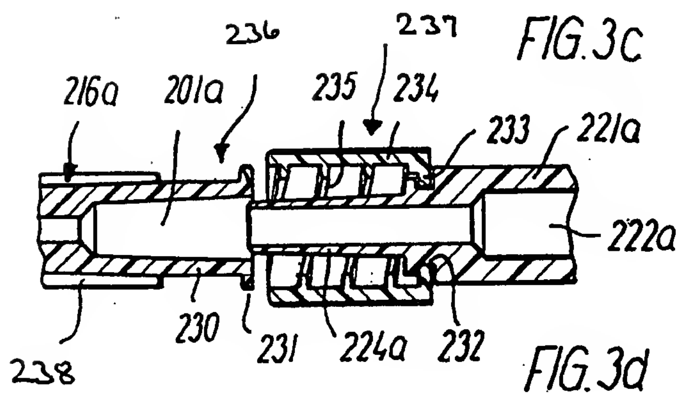

FIG.3d

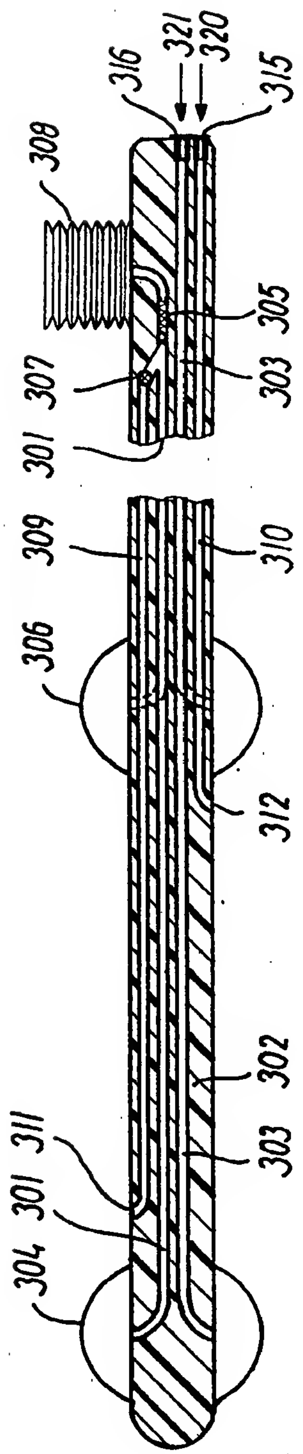
308
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FIG. 4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK 93/00239

A. CLASSIFICATION OF SUBJECT MATTER

IPC5: A61M 25/10
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC5: A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US, A, 4813935 (TERRY M, HABER ET AL), 21 March 1989 (21.03.89), see check valve 7, balloons 50, 8, 20 and 34, flushing ports 24, flushing channels 26 and adherent text	1-5,21-25,28
Y		6,7,9,10,18, 19,31
	--	
Y	US, A, 4116201 (NAYAN S. SHAH), 26 Sept 1978 (26.09.78)	6,7,9,10,21
A		1-5
	--	

[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents:
- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" erlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed
- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- "&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 October 1993	22-10-1993

Name and mailing address of the ISA/	Authorized officer
Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Leif Vingård Telephone No. +46 8 782 25 00

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK 93/00239

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO, A1, 8900059 (TERUMO KABUSHIKI KAISHA), 12 January 1989 (12.01.89), see spring coil valve 17 --	6,7,9
Y	US, A, 4439185 (INGEMAR H. LUNDQUIST), 27 March 1984 (27.03.84), see e.g. stop cocks 31 and 158, adjustment screw 131 and Luer fitting 157 --	10,19,31
Y	SE, B, 446656 (ASTRA MEDITEC AB), 29 Sept 1986 (29.09.86), see collecting means 21 --	18
Y	SE, B, 441979 (INGEVAR GUSTAFSON), 25 November 1985 (25.11.85) -- --------	20,22,24,32

INTERNATIONAL SEARCH REPORT

Information on patent family members

01/10/93

International application No.

PCT/DK 93/00239

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A- 4813935	21/03/89	NONE	
US-A- 4116201	26/09/78	CA-A- 1102651	09/06/81
WO-A1- 8900059	12/01/89	JP-A- 1008981	12/01/89
		JP-C- 1680363	13/07/92
		JP-B- 3046148	15/07/91
		JP-A- 1008980	12/01/89
		JP-B- 3018904	13/03/91
US-A- 4439185	27/03/84	CA-A- 1166919	08/05/84
		EP-A,B- 0054357	23/06/82
SE-B- 446656	29/09/86	AU-B- 582411	23/03/89
		AU-A- 5164385	17/07/86
		CA-A- 1271790	17/07/90
		DE-U- 8536508	13/03/86
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